REMARKS

Reconsideration is requested.

Claims 1-16 are pending. Claims 8-14 have been withdrawn from consideration.

The claims have been amended above, without prejudice.

To the extent not obviated by the above amendments, the Section 112, second paragraph, rejection of claims 3-7 and 15-16 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

Homologues are defined, for example, on page 7, lines 9-12, of the specification. The claim amendments in this regard are believed to be supported by the specification and the claims are submitted to be definite in the recitation of homologues. The claim recitation of specific hybridization is submitted to be definite.

One of ordinary skill in the art will appreciate from the specification as well as the generally advanced level of ordinary skill in the art that specifically hybridizes in the claims refers, for example, to hybridization to the recited target as opposed to random or non-specific hybridization. A "Quick Search" of the PTO on-line data base of granted patents indicates that the Patent Office has granted 614 patents from 1975 to date which contain the phrase "specifically hybridizes". Claim 1 of U.S. Patent No. 7,235,653, for example, provides the following:

"An antisense oligonucleotide which **specifically hybridizes** to a nucleic acid encoding human B7.2 protein, wherein the nucleotide sequence of said antisense oligonucleotide consists of SEQ ID NO: 391, and wherein said antisense oligonucleotide inhibits expression of said human B7.2 protein. "

Claim 19 of U.S. Patent No. 7,223,842, for example, provides the following:

"19. An antibody that binds specifically to an isolated polypeptide that is encoded by a 4.7 kb retinal mRNA transcribed from the q14 band of human chromosome 13, wherein said mRNA **specifically hybridizes** to a nucleic acid selected from the group consisting of p2AR0.9 and p2AR3.8. "

Claim 3 of U.S. Patent No. 7,192,786, for example, provides the following:

"3. The assay method according to claim 1, wherein the assay comprises a nucleic acid hybridization assay, in which the labelled bioaffinity reactant B comprises a nucleic acid probe which **specifically hybridizes** with the analyte. "

While the applicants have not reviewed the patents of the database in detail, the claims of the issued patents are submitted as evidence that one of ordinary skill, as apparently embodied by the applicants of the issued patents and the Patent Office examiner of the issued patents, understands and appreciates the metes and bounds of the objected-to phrase "specifically hybridizes".

For completeness, the applicants note that the present specification at page 5, lines 1-3, describes "taxon-specific hybridization" or "taxon-specific probe" as a probe that only hybridizes to the DNA or RNA from the taxon for which it was designed and not to DNA or RNA from other taxa.

Claim 3 no longer recites the objected-to broad and narrow ranges.

The objected-to phrase of claims 5-7 and 15 has been revised and is believed to be definite and will be understood by one of ordinary skill in the art.

As for the Examiner's objection-to the phrase "components necessary for producing said buffer", the applicants note that claims of the following nine (9) patents

which were revealed in a "Quick Search" of the PTO on-line database include the objected-to phrase:

U.S. Patent No. 7,195,765 Sequences of hepatitis C virus genotypes and their use as therapeutic and diagnostic agents[1];

U.S. Patent No. 7,150,875 Recombinant Plasmodium vivax merozoite protein-1 p42 vaccine[2];

U.S. Patent No. 7,060,276 Plasmodium falciparum AMA-1 protein and uses thereof [3];

U.S. Patent No. 7,026,457 Purified hepatitis C virus envelope proteins for diagnostic and therapeutic use[4] ;

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[1] Claim 10. A kit for determining the presence of HCV antigens present in a biological sample, said kit comprising: (a) at least one HCV antibody according to claim 1, (b) a buffer enabling the binding reaction between an HCV antibody of (a) and an HCV antigen present in said biological sample; or **components necessary for producing said buffer**, (c) a means for detecting the immune complexes formed between an HCV antibody of (a) and an HCV antigen present in said biological sample.
Primary Examiner: Housel; James
Assistant Examiner: Brown; Timothy

[2] Claim 8. A kit for determining the presence of malaria antibodies in a biological sample comprising: the protein according to claim 1, a buffer or **components necessary for producing a buffer**; and reagents for detecting immune complexes formed between the protein and antibodies present in the sample.
Primary Examiner: Minnifield; Nita
Assistant Examiner: Baskar; Padma

[3] Claim 10. A kit for determining the presence of malaria antibodies in a biological sample, comprising: a composition comprising the protein according to claim 3, a buffer or **components necessary for producing said buffer**; means for detecting immune complexes formed between the protein and antibodies present in the sample.
Primary Examiner: Smith; Lynette R. F.
Assistant Examiner: Baskar; Padma

[4] Claim 15. Kit for determining the presence of HCV antigens present in a biological sample, comprising: at least one E2 specific monoclonal antibody according to claim 1 or 2, a buffer or **components necessary for producing the buffer** enabling binding reaction between these antibodies and the HCV antigens present in said biological sample, a means for detecting the immune complexes formed in the preceding binding reaction.
Primary Examiner: Housel; James
Assistant Examiner: Li; Bao Qun

U.S. Patent No. 6,713,251 Method for detection of drug-induced mutations in the reverse transcriptase gene[5];

U.S. Patent No. 6,632,607 Mycobacterium antibiotic resistance detection[6];

U.S. Patent No. 6,245,503 Purified hepatitis C virus envelope proteins for diagnostic and therapeutic use[7];

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[5] Claim 1. A kit for inferring the nucleotide sequence at codons of interest in the HIV reverse transciptase (RT) and/or the amino acids corresponding to these codons and/or the HIV RT resistance spectrum of HIV isolates present in a biological sample comprising: (i) optionally, a means for releasing, isolating, or concentrating the polynucleic acids present in said sample; (ii) optionally, at least one suitable set of primers; (iii) at least two different probes, wherein each probe is capable of hybridizing specifically to one or more target codons within any region I to VIII as represented in FIG. 1, said probes optionally fixed to a solid support; (iv) a hybridization buffer, or **components necessary for producing said buffer**; (v) a wash solution, or components necessary for producing said solution; (vi) optionally, a means for detecting the hybrids resulting from the preceding hybridization; (vii) optionally, a means for attaching said probe to a solid support wherein the set of primers is selected from the group consisting of: SEQ ID No: 162 and 163, and SEQ ID No: 164 and 39.

Claim 2. A kit for inferring the nucleotide sequence at codons of interest in the HIV RT gene and/or the amino acids corresponding to these codons and/or the antiviral drug resistance spectrum of HIV isolates present in a biological sample, the kit comprising the following components: at least two different probes, wherein the probes are selected from the group consisting of SEQ ID NO: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34, 35, 37, 40, 41, 44, 45, 46, 47, 48, 49, 50, 51, 52, 54, 55, 56, 57, 58, 59, 61, 62, 63, 64, 65, 66, 67, 68, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 114, 115, 117, 118, 119, 120, 121, 122, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 138, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 154, 155, 156, 157 and 159; a hybridization buffer, or **components necessary for producing said buffer**; and a wash solution, or components necessary for producing said solution.

Primary Examiner: Horlick; Kenneth R.

[6] Claim 3. A kit comprising: (i) at least one oligonucleotide molecule consisting of a nucleotide sequence selected from the group consisting of: S11 (SEQ ID NO:2), S2 (SEQ ID NO:3), S3 (SEQ ID NO:4), S4444 (SEQ ID NO:8), S5 (SEQ ID NO:9), the RNA form of said SEQ ID NOs wherein T is replaced by U, and the complementary form of said SEQ ID NOs; (ii) a hybridization buffer, or **components necessary for producing said buffer**; and (iii) a wash solution, or components necessary for producing said solution.

Primary Examiner: Siew; Jeffrey

Assistant Examiner: Tung; Joyce

[7] Claim 1. Kit for detecting antibodies to HCV comprising:

at least one of an E1 protein and an E2 protein, said E1 protein and E2 protein having been purified to at least 80% pure; and

a buffer or **components necessary for producing a buffer** enabling formation of an immune complex between said protein and at least one of an anti-E1 antibody or anti-E2 antibody present in a biological sample, and

optionally, means for detecting said immune complex, and

optionally, at least one of an automated scanning or interpretation device for inferring a decrease of said anti-E1 antibody or anti-E2 antibody titers.

U.S. Patent No. 6,172,192 Toxoplasma gondii antigen Tg20 [8]; and

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Claim 15. Kit for detecting antibodies to HCV comprising an E1 protein of HCV and an E2 protein of HCV wherein at least one of said E1 protein and E2 protein has been purified to at least 80% pure; and

a buffer or **components necessary for producing a buffer** enabling formation of an immune complex between said protein and at least one of an anti-E1 antibody or anti-E2 antibody present in a biological sample, and

optionally, means for detecting said immune complex, and

optionally, at least one of an automated scanning or interpretation device for inferring a decrease of said anti-E1 antibody or anti-E2 antibody titers.

Primary Examiner: Allen; Marianne P.

Assistant Examiner: Zeman; Mary K

[8] Claim 6. A kit for detecting anti-T. gondii antibodies in a sample, said kit comprising:

at least one polypeptide or peptide according to claim 1, optionally in combination with other polypeptides or peptides being also optionally immobilized of a solid support,

optionally, a buffer, or **components necessary for producing the buffer**, enabling a binding reaction to occur between the antibodies present in said sample and said polypeptides or peptides,

optionally, a means for detecting the immune complex formed, and,

optionally, an automated scanning and interpretation device for inferring the presence of said antibodies in said sample.

Claim 24. A kit for detecting anti-T. gondii antibodies in a sample, said kit comprising:

at least one polypeptide or peptide according to claim 2, optionally in combination with other polypeptides or peptides being also optionally immobilized of a solid support,

optionally, a buffer, or **components necessary for producing the buffer**, enabling a binding reaction to occur between the antibodies present in said sample and said polypeptide or peptide,

optionally, a means for detecting the immune complex formed, and,

optionally, an automated scanning and interpretation device for inferring the presence of said antibodies in said sample.

Claim 25. A kit for detecting anti-T. gondii antibodies in a sample, said kit comprising:

at least one polypeptide or peptide according to claim 8, optionally in combination with other polypeptides or peptides being also optionally immobilized of a solid support,

optionally, a buffer, or **components necessary for producing the buffer**, enabling a binding reaction to occur between the antibodies present in said sample and said polypeptide or peptide,

optionally, a means for detecting the immune complex formed, and,

optionally, an automated scanning and interpretation device for inferring the presence of said antibodies in said sample.

Claim 26. A kit for detecting anti-T. gondii antibodies in a sample, said kit comprising:

at least one polypeptide or peptide according to claim 9, optionally in combination with other polypeptides or peptides being also optionally immobilized of a solid support,

optionally, a buffer, or **components necessary for producing the buffer**, enabling a binding reaction to occur between the antibodies present in said sample and said polypeptide or peptide,

optionally, a means for detecting the immune complex formed, and,

optionally, an automated scanning and interpretation device for inferring the presence of said antibodies in said sample.

Claim 27. A kit for detecting anti-T. gondii antibodies in a sample, said kit comprising:

at least one polypeptide or peptide according to claim 10, optionally in combination with other polypeptides or peptides being also optionally immobilized of a solid support,

optionally, a buffer, or **components necessary for producing the buffer**, enabling a binding reaction to occur between the antibodies present in said sample and said polypeptide or peptide,

optionally, a means for detecting the immune complex formed, and,

optionally, an automated scanning and interpretation device for inferring the presence of said antibodies in said sample.

Primary Examiner: Minnifield; Nita

U.S. Patent No. 5,721,097 Hybridization probes for the detection of branhamella catarrhalis strains[9].

The claims of the issued patents are submitted as evidence that one of ordinary skill, as apparently embodied by the applicants of the issued patents and the Patent Office examiner of the issued patents, understands and appreciates the metes and bounds of the objected-to phrase.

The claims are submitted to be definite and withdrawal of the Section 112, second paragraph, rejection is requested.

The Section 112, first paragraph "written description", rejection of claims 1-7 and 15-17 is believed to be obviated by the above amendments. Specifically, the claims relate to *S. aureus* and *S. aureus* specific fragments of the noted specifically recited sequences. The applicants submit that one of ordinary skill in the art will appreciate

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[9] Claim 12. A kit for the detection in vitro of Branhamella catarrhalis strains in a biological sample said kit comprising:

at least one rRNA related probe consisting of a sequence of at least 15 contiguous nucleotides to the maximum number of nucleotides of one of the following nucleic acid sequences: SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, or SEQ ID NO:8; or

a rRNA related probe hybridizing to a target consisting of at least 15 contiguous nucleotides to the maximum number of nucleotides of one of the following nucleic acid sequences: SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, or SEQ ID NO:8;

buffer or **components necessary for producing the buffer** enabling a hybridization reaction between these probes and the DNAs or RNAs of a strain of Branhamella catarrhalis; and

means for detecting the hybrids.

Claim 13. A kit for a sandwich hybridization assay to detect in vitro Branhamella catarrhalis strains in a biological sample, wherein said kit comprises:

at least two rRNA related probes targeting the same nucleic acid molecule, with at least one probe specific for Branhamella catarrhalis, wherein said probe is:

a probe consisting of a sequence of at least 15 contiguous nucleotides to the maximum number of nucleotides of one of the following nucleic acid sequences: SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, or SEQ ID NO:8; or

a probe hybridizing to a target consisting of a sequence of at least 15 contiguous nucleotides to the maximum number of nucleotides of one of the following nucleic acid sequences: SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, or SEQ ID NO:8;

buffer or **components necessary for producing the buffer** enabling a hybridization reaction between these probes and the DNAs or RNAs of a strain of Branhamella catarrhalis; and

means for detecting the hybrids.

from a review of the specification and the generally advanced level of skill in the art that the applicants were in possession of the claimed invention at the time the application was filed. Withdrawal of the Section 112, first paragraph "written description", rejection is requested.

The Section 102 rejection of claims 1-3, 7 and 15-16 over Jannes (U.S. Patent No. 6,312,903) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

Initially, the applicants request that the Examiner clarify or withdraw at least one of the Section 102 rejection, which alleges that the claimed invention was allegedly known in the art at the time the application was filed, or the seemingly contrary Section 112, first paragraph "written description, rejection which alleges that the applicants, who are expected to be in possession of the prior art, were not in possession of the claimed invention at the time the application was filed.

Substantively, the applicants note that the complementary sequences of the claims are complete complementary sequences, as opposed to the fragments and/or flanking sequences alluded to by the Examiner on page 10 of the Office action dated January 29, 2007. Claims 1, 2 and 7 are patentable over the cited patent, which fails to teach an isolated nucleic acid molecule consisting of SEQ ID NO: 1 or SEQ ID NO:2 of the present application, or an isolated nucleic acid molecule consisting of the complete complementary form of SEQ ID NO:1 or SEQ ID NO:2 of the present application, or an isolated nucleic acid molecule consisting of the RNA form of SEQ ID NO:1 or SEQ ID NO:2 or an isolated nucleic acid molecule consisting of the RNA form of the complete

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Primary Examiner: Houtteman; Scott W.

complementary form of SEQ ID NO:1 or SEQ ID NO:2 of the present application, or a composition containing any of these. The 383 base pair sequence of SEQ ID NO:142 of the cited patent fails to anticipate the presently claimed invention.

With regard to claim 3 of the present application, the applicants note that the 383 base pair sequence of SEQ ID NO:142 of the cited patent, which the Examiner has identified, will not specifically hybridize to SEQ ID NO:1 or 2 of the present claims, or function to meet the other specific hybridization conditions of claim 3 because the sequence contains additional 240 bases which one of ordinary skill would understand to provide non-specific hybridization to sequences other than the sequence described in claim 3.

With regard to the STAU-ICG1 probe (SEQ ID NO:53) of the cited patent identified by the Examiner on page 11 of the Office Action dated January 29, 2007, the applicants urge the Examiner to see column 80, lines 52-53 of the cited patent wherein the patentee describes SAU-ICG1 as reacting "with all Staphylococcus spp. tested". SEQ ID NO:53 of the cited patent is not a S. aureus specific sequence or fragment of the present claims.

Claims 15 and 16 are submitted to be patentable over the cited patent for reasons noted above with regard to claims 1, 2, 3 and 7.

Withdrawal the Section 102 rejection of claims 1-3, 7, 15 and 16 over Jannes is requested.

The Section 103 rejection of claims 4-6 over Jannes is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following distinguishing comments.

The sequences of SEQ ID NOs: 1 and 2 of the claims, as well as S. aureus specific sequences therefrom of the claims were not obvious in view of the cited patent which includes, for example, the 383 base sequence noted by the Examiner.

As noted above, the specific 30 base sequence of the patent identified by the Examiner (i.e., SEQ ID NO:53) was not a S. aureus specific sequence. Beyond the non-specific sequence referred to by the Examiner, the cited patent teaches in Example 9 the use of a sequence STAU-IG2 which cross-hybridized with S. lugdinensis and two further sequences which failed to detect all S. aureus strains tested.

The cited patent does not teach or suggest the presently claimed invention as a predictable alternative to the non-specific sequences of the cited patent.

Bacterial species, and in particular Staphylococcus species, harbor multiple ribosomal spacer regions in their circular genome. Within Staphylococcus species, and in particular Staphylococcus aureus, these spacer regions can differ in length and sequence.

The selection of the sequences SEQ ID NOs: 1 and 2 has been carefully made after comparison of different spacer regions of many different Staphylococcus species. Based on these sequence data, the unique character of this region was detected and discovered by the applicants, since the region is present in the different spacer regions of the most clinical relevant Staphylococcus species and can be amplified with a single primer pair.

Furthermore, the great advantage of the method of the present invention is that it is surprisingly highly sensitive (see page 5, lines 9-10 of the specification). The claimed invention is able, with a very high sensitivity, to detect the presence of a clinically

relevant Staphylococcus and to identify the presence of Staphylococcus aureus in a sample (see page 36, lines 10-20 of the specification).

As discussed above, the method of present invention can achieve high selectivity in both the detection and identification and high specificity in identification. It should not be underestimated that it is capable of said achievement using much more conserved spacer region than is described in the cited patent.

The sequences of the presently claimed invention are present in all Staphylococcus aureus strains since they were selected from a more conserved part available in all spacer types, while in the cited patent unique probes were selected from more variable regions from different spacer types not available in every strain. For this latter reason, a combination of more than one sequence is needed in the cited patent to detect all Stahpylococcus aureus isolates.

The applicants note, for completeness, that the recitation of a set of two probes in the present invention relates to the technology employed, such as FRET (fluorescence resonance energy transfer) or hybridization probe technology in combination with the light-cycler. Both probes, adjacent to each other are needed for the generation of fluorescent light emission and both contribute to the specificity and selectivity of the probe system for identification of Staphylococcus aureus.

The claims are submitted to be patentable over the cited patent and withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

Respectfully submitted,

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